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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR		ATTORNEY DOCKET NO.
09/036,819	03/09/98	SHAMI	A	107-145D-C

HM12/1202

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1641	12

DATE MAILED: 12/02/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/036,819	Applicant(s) El Shami
	Examiner S. Devi, Ph.D.	Group Art Unit 1641

☒ Responsive to communication(s) filed on *Oct 28, 1999* .

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *42-53* is/~~are~~ pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *42-53* is/~~are~~ rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☒ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Request for Continued Prosecution Application

1) The request filed 10/28/99 (paper no. 10) for a Continued Prosecution Application (CPA) under 37 C.F.R 1.53(d) based on the parent Application, SN 08/036,819, is acceptable and a CPA has been established. An action on the CPA follows.

It is noted that no preliminary amendment has been submitted along with the request filed for the CPA.

Priority

2) The instant application has been filed as a Continuation of application SN 07/303,712, filed 01/27/89, now abandoned, which is a Divisional application of SN 06/784,857, filed 10/04/85, now abandoned.

Prosecution History of Parent Applications

3) It is noted that the grand parent application, SN 06/784,857, was involved in an Interference (# 101, 933) and a judgement adverse to the Applicant was rendered.

It is noted that claims similar to the ones that are pending in this application, were rejected in the parent case, SN 07/303,712, based on the interference count, which rejection was affirmed by the Board.

Status of Claims

4) Claim 41 is canceled via the amendment filed 09/20/99 (paper no. 7).

New claim 53 is added via the amendment filed 09/20/99 (paper no. 7).

Claims 42-52 have been amended via the amendment filed 09/20/99 (paper no. 7).

Claims 42-53 are pending in this application and are under examination.

Prior Citation of Title 35 Sections

5) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

6) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been

previously cited and made of record.

Drawings - Objection Moot

7) In response to the objection to the drawings made in paragraph 5(c) of the Office Action mailed 02/04/99 (paper no. 4) and maintained in paragraph 9 of the Office Action mailed 06/24/99 (paper no. 6) under 37 C.F.R 1.84, Applicant has canceled all the drawings via the amendment filed 09/20/99 (paper no. 7). The objection is moot.

Specification - Objection Moot

8) The objection to the specification made in paragraph 5(c) of the Office Action mailed 02/04/99 (paper no. 4) and maintained in paragraphs 7 and 9 of the final Office Action mailed 06/24/99 (paper no. 6) with regard to the lack of the section: "Brief Description of the Drawings" in the specification and lack of reference to the Figures, is moot in light of Applicant's cancellation of all the drawings via the amendment filed 09/20/99 (paper no. 7).

Specification - Objection Maintained

9) The objection to the specification made in paragraph 5(b) of the Office Action mailed 02/04/99 (paper no. 4) and maintained in paragraph 8 of the final Office Action mailed 06/24/99 (paper no. 6) is maintained for reasons set forth therein. Although Applicant has replaced Tables 20-25 via the amendment filed 04/12/99 (paper no. 5), the rest of the Tables and related text have not been amended. However, Applicant assures the Office that the specification would be appropriately edited upon indication of allowance.

Rejection Moot

10) The rejection of claims 41-52 made in paragraph 15 of the final Office action mailed 06/24/99 (paper no. 6) under 35 U.S.A. 112, first paragraph, as containing new matter, is moot in light of Applicant's cancellation of the base claim 41.

New Rejections

The Applicant is asked to note the new rejections made in this Office Action. Applicant's amendment necessitated the new grounds of rejection presented in this Office Action.

Rejections - 35 U.S.C § 102

11) The following is a quotation of the appropriate paragraphs of 35 U.S.C § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (e) The invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

12) Claims 53, 42-44, 46 and 48-50 are rejected under 35 U.S.C § 102(e) as being anticipated by Midgley *et al.* (US 4,366,143) ('143).

Midgley *et al.* disclose a method of determining the concentration of a free ligand in a biological fluid in the presence of the ligand bound to natural binders for the ligand (i.e., endogenous binding proteins) wherein the bound and the free ligand are in equilibrium with one another. The method comprises of admixing a sample of the biological fluid: 1) with an amount of a labeled derivative of the ligand (i.e., the ligand analog tracer), which is non-reactive (non-binding to) with the natural binders, and 2) an amount of a specific binder for the ligand, effecting the reaction between the free ligand, the labeled derivative and the specific binder, separating the labeled derivative bound to the specific ligand binder from the unbound labeled derivative, measuring the amount of the labeled derivative of the ligand bound to the specific binder and using the measurement to determine the concentration of free ligand in the biological fluid (see abstract and claim 10). A specific blocking agent, i.e., specific inhibitor agent, that inhibits the binding of the labeled ligand derivative to the natural binder or the endogenous protein, may be added (see the second paragraph of column 11). The free ligand measured is testosterone (see claim 3 and the first full paragraph in column 9). The specific ligand binder is an antibody to the free ligand (see claim 4) which is immobilized on a solid substrate or support such as polystyrene latex (see claim 13 and lines 35-38). The ligand derivative (i.e., the ligand analog tracer) is labeled with a fluorophor, a light chromophore, an enzyme or a chemiluminescent group, or a radioactive atom (see lines 25-30 of column 4). The method is carried out at 37°C and at a pH of 7.4 (see claim 16 and Examples 6 and 7). The blocking agent (i.e., the specific inhibitor agent) used in the method can be 8-anilinonaphthalene sulphonic acid or ANS, i.e., a dye (see Example 4). The concentration of free ligand in the biological fluid is calculated using a number of standard sera of known free ligand content determined by equilibrium dialysis spanning the

required working range of the method. The results are plotted graphically and unknown samples are read off against the curve (see lines 3-23 of column 5).

Claims 53, 42-44, 46 and 48-50 are anticipated by Midgley *et al.* ('143).

13) Claims 53, 42, 43 and 52 are rejected under 35 U.S.C § 102(a) as being anticipated by Midgley *et al.* (EP 0,155,104) ('104).

Midgley *et al.* ('104) disclose a method of determining the concentration of a free analyte (i.e., ligand) in a biological fluid which also contains the analyte bound to one or more natural binders for the analyte (i.e., endogenous proteins), the bound and free analyte being in equilibrium with one another, by reacting the biological fluid with an amount of a specific binder such as an antibody for the analyte insufficient to affect the equilibrium and with an amount of a labeled derivative of the analyte or analogue tracer having a lower affinity for the natural binders than for the analyte and a differential blocking agent (i.e., specific inhibitor agent) which substantially reduces the binding of the analyte derivative to the natural binder, maintaining the mixture for a time to permit the free portion of the analyte derivative to compete for binding with the specific binder, measuring the amount of analyte derivative that has, or has not, become bound to the specific binder, and using the measurement to determine the concentration of free analyte in the biological fluid (see claims, page 8, lines 9-12 and page 3). The analyte or ligand can be testosterone (see page 7). The various blocking agents used in the method are disclosed including oleic acid (see page 11 and Example 5), salicylic acid, barbital, 5-sulphosalicylic acid, gentisic acid, gamma-resorcylic acid and 2, 4-dinitrophenol (see claim 4 and Table 9).

Claims 53, 42, 43 and 52 are anticipated by Midgley *et al.* ('104).

Rejections under 35 U.S.C § 103(a)

14) Claim 45 is rejected under 35 U.S.C § 103(a) as being unpatentable over Midgley *et al.* (US 4,366,143) ('143) as applied to claim 53 above, and further in view of Hertl *et al.* (GB 2 085 160 A).

The teachings of Midgley *et al.* ('143) have been explained above, which do not expressly disclose the use of a polypropylene solid substrate.

However, Hertl *et al.* disclose polypropylene as an alternative solid substrate to polystyrene for use in the immobilization of a specific binder such as an anti-ligand antibody that

is used in a method of measuring the concentration of a free ligand in a liquid sample (see page 4, left column and claims).

It would have been obvious to one skilled in the art at the time the invention was made to replace Midgley's ('143) polystyrene solid substrate with Hertl's polypropylene substrate to produce the instant invention, with a reasonable expectation of success, because Hertl *et al.* teach that it is conventional to use polypropylene as an alternative substrate to polystyrene for antibody immobilization for use in a method of measuring the concentration of a free ligand in a liquid sample. One would have had a reasonable expectation of success in obtaining the method of the instant invention by using polypropylene as an alternative, functionally equivalent solid substrate to Midgley's polystyrene, since such a substitution would be expected to yield similar results, absent a showing that polypropylene would function significantly differently than polystyrene in immobilization of the antibody.

Claim 45 is *prima facie* obvious over the prior art of record.

Rejection Based on the Lost Interference Count

15) In accordance with the practice set out in M.P.E.P 2363, claims 42-53 are rejected under 35 U.S.C § 103 as being unpatentable over the count of Interference no. 101,933.

The count 1 of Interference no. 101,933 is provided below:

> In a method of determining the concentration of a free portion of a ligand in a biological fluid, wherein said free ligand is in equilibrium with another portion of the ligand bound to one or more endogenous binders in said fluid comprising the steps of (a) forming a mixture of a sample of said fluid with (1) an amount of a specific binder for the free ligand insufficient to substantially affect said equilibrium, and (2) a labeled derivative of the ligand that binds to said specific binder and has affinity for the endogenous binders lower than that of the ligand for said endogenous binders, (b) maintained said mixture to permit the ligand derivative to complete with the free ligand for binding with the specific binder, (c) measuring the amount of ligand derivative that has, or has not, become bound to the specific binder, and (d) determining the concentration of said free ligand from said measurement, wherein the improvement comprises including in the mixture an amount of a blocking agent which substantially reduces the binding of the ligand derivative to the endogenous binders without substantially reducing the binding of the ligand to said endogenous binders.

The count clearly embraces the use of a specific binding ligand in a method of determining or measuring the concentration of any free ligand in a biological fluid. The free ligand in the count is inclusive of the testosterone ligand (subgenus) now recited in instant claims and therefore, instant claims are unpatentable or obvious over the count of Interference no. 103,933.

It is noted that a similar rejection made in the parent case, SN 07/303,712, was affirmed

by the Board.

Remarks

16) Claims 42-53 stand rejected.

17) Papers related to this application may be submitted to Group 1600, AU 1641 by facsimile transmission. Papers should be transmitted via the PTO Fax Center located in Crystal Mall 1 (CM1). The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The CM1 facsimile center's telephone number is (703) 308-4242.

18) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (703) 308-9347. The Examiner can normally be reached on Monday to Friday from 8.00 a.m to 4.00 p.m.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, James Housel, can be reached on (703) 308-4027.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

December 1999

James C. Housel
JAMES C. HOUSEL 12/2/99
SUPERVISORY PATENT EXAMINER